UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,761	11/06/2001	Peter F. Searle	CACO-0067(P21303US)	9242

7590 03/23/2004

Robin S Quartin
Woodcock Washburn Kurtz
Mackiewicz & Norris
One Liberty Place - 46th Floor
Philadelphia, PA 19103

EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,761	SEARLE, PETER F.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-17 with the species nitrodeductase for the activating enzyme, CB 1954 as the prodrug, antibiotic resistance marker is acknowledged. The traversal is on the ground(s) that Group I and IV should be examined concurrently. Applicants however, recognize that Group IV is to a method of cloning as opposed to Group I method of selecting nucleic acid encoding enzyme. Applicant further traverses that both groups belong to the same class. And, that no burden would be imposed on the Office to examine both groups. This is not found persuasive because Group IV does not only include the additional step of cloning, as admitted, but also other components and fragments of the enzyme. Although each of these groups belong to the same class however, each belongs to a different subclass. Examination of both groups will indeed impose a burden. The search is not limited to U.S. Patent searches but to scientific journals, as well. These searches are not co-extensive.

The requirement is still deemed proper and is therefore made FINAL.

Claims 18-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected

invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

Status of Claims

Claims 1-21 are pending

Claims 18-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 1-17 are under examination.

Specification

The abstract of the disclosure is objected to because of the used of phraseology "comprises" often used in patent claims. Correction is required. See MPEP § 608.01(b).

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and

use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide an adequate written description for a method that uses any type of prodrug, an enzyme that cleaves said prodrug and a bacteriophage library. The disclosure provides general statement as generic as that claimed. However, the specifics or details of the description are drawn only to the single enzyme nitroreductase that cleaves specifically the prodrug, CB1954. The specificity action of an enzyme is clearly evident from the experiments conducted in the specification. The conditions and components employed in the method are for the components that are specifically under study. The disclosure lacks any reasonable assurance as to the experimental

conditions, the enzymes, the cleavable prodrug and other unpredictable factors applicable relative to the experiments used herein. It is well known in the art that compounds expressed in the library may at times are not true representation of all the compounds. See Fischetti et al (6,238,661), specifically at col. 2, lines 1-14. See University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (DC WNY 2003).

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 5 recitation of "other selectable marker" is indefinite as to what is included or excluded by the term "other", especially in the absence of positive description in the specification.

2. Claim 10 is indefinite as to alternative conditions employed for and/or phrase.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5 and 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Maruyama et al (2002/0110802).

Maruyama et al discloses at col. 10, [0157] a method for producing a biologically active multimeric polypeptide complexes generally involves (1) preparing a polypeptide-encoding gene and inserting the gene into a lambdoid bacteriophage vector of this invention using genomic DNA or cDNA as a source for the DNA inserts, (2) expressing the fusion protein containing the polypeptide-encoding gene in said vectors capable of expressing and assembling a multimeric polypeptide molecule on the surface of a lambdoid phage particle, and (3) alternatively (i) isolating the surface-expressed phage particle using immunoaffinity techniques such as panning of phage particles

against a preselected biological binding activity, thereby isolating one or more species of phage containing particular polypeptide-encoding genes and protein molecules that have the desired biological binding activity, or (ii) isolating the surface-expressing phage particle using enzymatic techniques such as contacting the phage particle with a preselected substrate, maintaining the phage-substrate under conditions favoring catalysis, and detecting the formation of products, thereby identifying one or more species of phage containing particular polypeptide-encoding genes and protein molecules that catalyze a preselected enzymatic reaction. See col.11, [0162] for the random mutagenesis. See also, col. 7, [0107]; col. 9, [0138] up to [0142]; col. 10, [0155]; col. 14, [0213] and specifically the Examples at col. 28 up to col. 35

Accordingly, the method of Maruyama using specific enzymes in a bacteriophage that catalyzes the beta galactoside fully meets the broad scope of the claimed method. The claimed proteolytic activity of the bacteria is a property inherently contained in the bacteria of Maruyama.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over McNeish (Gene Therapy) in view of Maruyama et al or Murray(Phages).

McNeish et al discloses at page 1061, abstract a method of selecting nucleic acid encoding an enzyme, nitroreductase, that cleaves the prodrug, CB1954. The method comprises expressing of the E. coli enzyme nitroreductase (NTR) in tumor cells that enable them to activate the prodrug CB1954 that leads to interstrand DNA crosslinking (i.e.,lysogenic state, as claimed) and cell death. Using transfected or retrovirally transduced cells, the expressed nitroreductase is selected and determined as to its cleavage of CB1954. The generation of the pooled populations is described at col. 2. See the specifics of the method at page 1067, section Materials and Methods heading. McNeish does not disclose the use of bacteriophage library

containing the enzyme to transduce the cells. However, Murray discloses at page 411, that in principle, a random population of DNA fragments can be recovered in a phage. The construction of truly representative libraries of any genome required randomly fragmented DNA. Murray at page 395 discloses that transducing phages facilitated functional and structural analyses of bacterial genes. At page 15 Murray discloses that gene claimed in page, particularly lambda may be studied with the phage in either the lytic or the lysogenic mode. In the lysogenic mode, a single copy of a cloned gene per bacterial chromosome can be maintained thereby minimizing some selective pressure. Furthermore, at page 424 Murray disclose that lambda vectors are commonly used for making genomic libraries since large DNA fragments are recovered efficiently. See Maruyama as discussed above and the advantages derived in the use of bacteriophage. It would have been obvious to one having ordinary skill in the art at the time the invention was made to use bacteriophage as the vector in the method of McNeish in the manner as taught by Murray or Maruyama. The numerous advantages derived in the use of said phage especially in a bacterial host as taught by Murray or Maruyama provides the motivation to one having ordinary skill in the art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on(571) 272-0812. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
March 22, 2004